Development of the Decision Support System in Treatment of Arterial Hypertension

Application of Artificial Neural Networks for Evaluation of Heart Rate Variability Signals

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Abstract: The article presents first step of the decision support system development in treatment of arterial hypertension. Results of arterial hypertension diagnostic task by short-term signals of heart rate variability are presented. The tilt test study was used as the functional load. The peculiarity of this work is application of neural networks for this task. The different number of hidden layers in the neural networks and different number of neurons in hidden layers were tested in this study. The classification accuracy of the neural networks was compared with those of simple machine learning classifiers. The following steps of the decision support system development are declared.

1 INTRODUCTION

According to the WHO experts the arterial hypertension is the most frequent pathology of cardiovascular system. It is occurring among 15-25% of adult population. Hypertension is one of the most important factors of such diseases as coronary heart disease, stroke and heart failure. The arterial hypertension has a multi-factor origin and for a long time is asymptomatic. However, fairly soon it might lead to acute events. Therefore the task of early preclinical diagnostic is relevant (Feng et al., 2014; Mancia et al., 2013; Mendis et al., 2010).

The arterial hypertension emerges as a result of regulatory mechanisms disorders of the vascular tone. The most important indicator of the vascular tone is the arterial pressure. It is well known that arterial pressure is supported by the several regulatory mechanisms, including neuronal and humoral. Here is the exceptional role of the autonomic nervous system (ANS).

Often, in accordance with recommendations of the medical societies, arterial hypertension treatment consists of several medications. These may lead to polypragmasy and several side effect (Mancia et al., 2013). The alternative to the pharmacological approach is application of the physiotherapy equipment dedicated to improvement of the cardiovascular system. The 'SYMPATHOCOR-01' neuro-electrostimulator is one of such devices. The device provides correction of the sympathetic department of the ANS. Through the sympathetic department the device has constricted control of the vascular tone (Kublanov et al., 2010). Thereby it is appropriate to apply in the development of the decision support system in treatment of arterial hypertension such methods that allow monitoring current state of the ANS.

One of the indirect ways to access functioning of the ANS is the heart rate variability (HRV). (Kseneva et al., 2016). Non-invasiveness and easy derivation of the HRV measurement make it widely studied and practical tool to monitor ANS function (Zadeh et al., 2010). The R-R intervals of the ECG signals forms the Heart Rate Variability (HRV) signals. The digital HRV signal processing has a long history and methodological recommendation for practical usage were reflected in work of various scientific groups in many countries around the globe (Malik, 1996; Tarvainen et al., 2014; Ushakov et al., 2013).

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In some works authors suggest that common features of HRV have low sensitivity. However, joint application of common features with non-linear estimations could be of great benefit for more practical identification of patients at risk (Chattipakorn et al., 2007)

The Artificial Neural Networks (ANN) Artificial neural networks is a computing approach, which was inspired by the functioning of the biological neural networks. Such approach have proven to be successful in solving different task on variety of data(Belova et al., 2007; Lee et al., 2005; Tkacz and Kostka, 2000). There are several works in which ANN is applied for HRV signals computing (Patel et al., 2011; Rajendra Acharya et al., 2003). However, in that works a limited number of HRV features were used.

On the other hand, there are works that apply ANN for classification of arterial hypertension among people suffering from obesity (Pytel et al., 2015). There, anthropometric measures were used as the hypertension indicators. However such approach does not allows to evaluate dynamic reaction of the organism on the functional load.

To our knowledge this study is the first attempt to apply ANN for diagnostic of the arterial hypertension using big vector of the HRV features. The goal of the present work is first stage in the development of the decision support system in treatment of arterial hypertension. For this in present work classification accuracy of ANN was evaluated for two groups – relatively healthy volunteers and patients suffering from arterial hypertension. Additionally, obtained results were compared with evaluations of other machine learning classifiers.

2 MATERIALS AND METHODS

2.1 Clinical Data

The clinical data was recorded at the Sverdlovsk Clinical Hospital of Mental Diseases for Military Veterans (Yekaterinburg, Russian Federation). This pilot study had an approval of the local Ethics Committee (Ural State Medical University, Yekaterinburg, Russian Federation). The dataset itself includes the recorded data of 28 healthy people and 40 patients. All the patients were diagnosed with the II/III degree of arterial hypertension. All participants were volunteers and had signed the participation consent.

The exclusion criteria were: liver failure, kidney failure, diabetes of I type, diffusion collagen disease, heart failure of III-IV class (NYHA classification), respiratory failure, acute impairment of cerebral circulation (6 month prior to the study), unstable angina or myocardial infarction (6 month prior to the study), permanent atrial fibrillation, women during pregnancy and lactation period.

Electrocardiography (ECG) signals were recorded by the electroencephalograph-analyzer “Encephalan-131-03” (“Medicom-MTD”, Taganrog, Russian Federation) in the first limb lead (Kleiger et al., 2005). After the ECG signal recording the “Encephalan-131-03” software automatically derive the HRV signals.

The clinical data was recorded in three functional states involving the rotating table Lojer (Vammalan Konepaja DY, Finland). During the first state the participant calmly lies on the exanimating table (state F). At the second state the so-called tilt-test is performed – the head end of the table is lifted up to 70º from the horizontal position (state O). At the final state the participant returns to the horizontal position (state K). The functional load was supervised by the physician. The duration of the signal record in each state was 300 seconds. In this study only features of state O were used, as this state was the most efficient classification accuracy wise (Kublanov et al., 2017).

2.2 Heart Rate Variability Features

Usually in state-of-art works that involve HRV signal processing the Kubios software package is used to extract HRV-related features (Tarvainen et al., 2014). Tables 1-6 present summary of the features used in this study. That list of features consist of time-domain (tables 1 and 2) and frequency-domain features (table 3) established by the European Society of Cardiology (Malik, 1996) as well as relevant non-linear features (table 4) (Sivanantham and Shenbaga Devi, 2014). In our study, in addition to commonly used features, the wavelet transform features were used (tables 5 and 6) (Egorova et al., 2014). Overall, a comprehensive list of 64 features was considered.

Before features calculation, the outliers were removed from the original R-R time series. By outliers in this study, we have considered values of R-R time series that differed from the mean of time-series by more than three times of the standard deviation. Across the entire signal samples less than 1.7 % of data were removed. This processed version of the signal will be referred as a *NN* (Normal-to-Normal) time series.

Table 1: HRV statistical features.

Feature	***Description***
M	Mean value of the NN time-series
HR	Heart Rate
SDNN	Standard Deviation of the NN time-series
skewness	Skewness of the NN time-series
kurtosis	Kurtosis of the NN time-series
CV	the Coefficient of Variation
RMSSD	Square Root of the Mean of Squares of the NN time-series
NN50	Variation higher than 50ms in the NN time-series
pNN50	Normalized NN50 by the length of NN time-series
SDSD	Standard Deviation of Differences between Successive elements in NN time-series
ZCR	Zero Crossing Rate

Statistical features included general estimation, like mean and standard deviation. Moreover, there were HRV-specific ones, which concern interaction between consequent intervals (Malik, 1996). In table 1 the ZCR feature is evaluated in relation to the mean value of the NN time series.

Table 2: HRV geometric features.

Feature	***Description***
M0	Mode of the NN time-series
VR	Variation Range
AM0	Amplitude of the Mode
SI	Stress Index
IAB	Index of Autonomic Balance
ARI	Autonomic Rhythm Index
IARP	Index of Adequate Regulation Processes
St. George Index	The triangular Index

In table 2 the standard features are the mode, amplitude of the mode, variation range and St. George Index (Malik, 1996). Remaining features are calculated using the standard ones, in accordance with recommendations (Baevskiy, 2001).

In the case of the Fourier and wavelet transform evaluation, the original R-R intervals were interpolated, for a corresponding sampling frequency of 10Hz, using cubic splines before the spectral analysis (De Boor, 1978). For the wavelet transform computation the Gaussian wavelet of the 8-th order was used (Mallat, 2009). Main frequency components of HRV are: high frequency (HF), from 0.15 to 0.4 Hz; low frequency (LF), from 0.04 to 0.15 Hz; very low frequency (VLF), from 0.003 to 0.04 Hz.

Table 3: HRV Fourier spectral features.

Feature	***Description***
HF(Fr)	High Frequency Fourier Spectral Power
LF(Fr)	Low Frequency Fourier Spectral Power
VLF(Fr)	Very Low Frequency Fourier Spectral Power
TP(Fr)	Total Power of the Fourier Spectrum
LF/HF(Fr)	Autonomic Balance Exponent Power of the Fourier Spectrum
HFmax(Fr)	Maximum power of the HF
HFn(Fr)	Normalized Power of the HF Fourier Spectrum
LFn(Fr)	Normalized Power of the LF Fourier Spectrum
VLFn(Fr)	Normalized Power of the VLF Fourier Spectrum
IC	Index of Centralization
IAS	Index of the Subcortical Nervous Center's Activation
HFmax	the maximal power of the HF spectral component
RF	Respiration Frequency
LFmax	the maximal power of the LF spectral component
f(LFmax)	the frequency that corresponds to the LFmax
VLFmax	the maximal power of the VLF spectral component
f(VLFmax)	the frequency that corresponds to the VLFmax

In table 4 the SD1 and SD2 values are evaluated for the Poincare plot – graph of the NN time-series, when each interval is plotted against the following interval. The Entropy indexes are indicators of the time series complexity and regularity (Yentes et al., 2013).

Table 4: HRV non-linear features.

Feature	***Description***
En	Shannon entropy
EnInterp	Shannon entropy of the interpolated time-series
ApEn	Approximate Entropy
SamEn	Sample Entropy
SD1	Standard Deviation perpendicular the line-of-identity
SD2	Standard Deviation along the line-of-identity
SD1/SD2	Ratio of Poincare Plot's Standard Deviations

In table 5, in addition to the common HRV spectral features, the Standard Deviations and Shannon entropies of the time series, obtained by the wavelet transform are presented.

Table 5: HRV wavelet spectral features.

Feature	*Description*
HF(wt)	High Frequency Wavelet Spectral Power
LF(wt)	Low Frequency Wavelet Spectral Power
VLF(wt)	Very Low Frequency Wavelet Spectral Power
TP(wt)	Total Power of the Wavelet Spectrum
HFn(wt)	Normalized Power of the HF Wavelet Spectrum
LFn(wt)	Normalized Power of the LF Wavelet Spectrum
VLFn(wt)	Normalized Power of the VLF Wavelet Spectrum
LF/HF(wt)	Autonomic Balance Exponent Power of the Wavelet Spectrum
mHF(wt)	Mean High Frequency Wavelet Spectral Power
mLF(wt)	Mean Low Frequency Wavelet Spectral Power
mVLF(wt)	Mean Very Low Frequency Wavelet Spectral Power
SDHF(wt)	Standard deviation of the HF(t) Wavelet time series
SDLF(wt)	Standard deviation of the LF(t) Wavelet time series
SDVLF(wt)	Standard deviation of the VLF(t) Wavelet time series
EnHF(wt)	Shannon entropy of the HF(t) Wavelet time series
EnLF(wt)	Shannon entropy of the LF(t) Wavelet time series
EnVLF(wt)	Shannon entropy of the VLF(t) Wavelet time series

Table 6 presents features of the (LF/HF)[t] informational characteristics. (LF/HF)[t] is the continuous function of the LF/HF ratio, obtained by means of the wavelet analysis. Local dysfunctions of this function represent relevant information of the functional changes during the loads. The effectiveness of such features was shown previously in (Egorova et al., 2014).

Table 6: HRV wavelet dysfunctions features.

Feature	*Description*
(LF/HF)max	Maximal value of dysfunctions
(LF/HF)int	Intensity of dysfunctions
Nd	Number of dysfunctions
pNd	the number of dysfunctions divided by the length of the (LF/HF)[t].

All 64 features for all 68 subjects have formed single matrix of features X (matrix size 68x64). In addition, the class matrix was created (matrix size 68x2): for relatively healthy volunteers the line in matrix is (1,0); for patients suffering from arterial hypertension is (0,1).

2.3 Artificial Neural Networks

The ANN learn a set of parameters that are adjusted to the input data, while comparing the their prediction with the output in the training phase. In current work, several Multilayer Perceptrons (MLP) with different number of hidden layers and neurons were considered. The general view of the used neural networks structure is presented on figure 1.

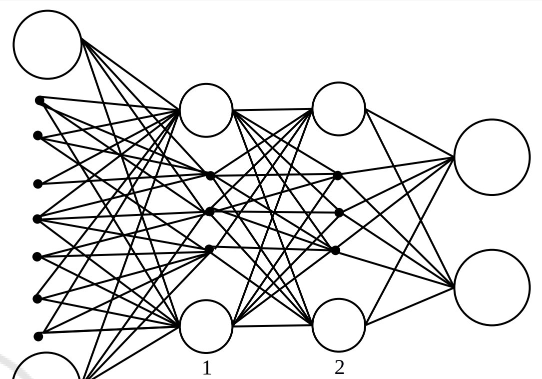

Figure 1: Neural networks schematic.

Neural networks were used as the classifier: based on the input matrix X the network is expected to define affiliation to either group of healthy volunteers or patients suffering from arterial hypertension. Input layer consists of 64 nodes – neurons. Each node represents one of the considered heart rate variability features. Prior to feeding the features to the network, the feature vector was normalized to have a zero mean value and uniform standard deviation (Sola and Sevilla, 1997).

Output layer consisted of 2 neurons; one neuron is responsible for defining affiliation to group of healthy volunteers, second is responsible for defining affiliation to the group of patients. Therefore, the network is expected to give an answer (1,0) if the subject belongs to the group of healthy volunteers, and to give an answer (0,1) if the subject belongs to the group of patients suffering from the arterial hypertension. The number of neurons in the hidden layers varied. Two types of neural networks were analyzed: with one hidden layer, and with two hidden layers. In addition number of neurons in each layer varied from 1 to 64.

In order to define weights and biases the back propagation method was used. The learning method was set to be 0.1. As the stopping criteria the maximal error level was used, which should not suppress 0.01.

Maximal number of iterations was set to be 10000. However, all networks configuration converged prior. As the activation function the logistic function was used. One of the features of this function is relative easiness of prime evaluation (Demuth et al., 2014; Hornik et al., 1989; Schmidhuber, 2015) .

In order to evaluate efficacy of the network configuration, the leave-one-out cross-validation (LOOCV) technique was used. LOOCV is the so-called exhaustive cross-validation type which uses one of the observations in the dataset as the test set, while remaining data is used as the training set. This procedure is repeated for all the observations in the dataset (Refaeilzadeh et al., 2009). The total accuracy (ACC) is evaluated as the number of correctly predicted test set during whole LOOCV application. Using the LOOCV approach allows one to prevent overfitting on the training set while evaluating classification efficacy on the external data.

3 RESULTS

In our previous works (Kublanov et al., 2017) we have analyzed the following machine learning classifiers – linear and quadratic discriminant analysis (LDA and QDA); k-nearest neighbors (k-NN), for k = 3,4,5; Decision Tree (DT) and Naïve Bayes (NB). The table presents results of the classification using all features for different classifiers.

Table 7: Classifiers accuracy, %.

LDA	QDA	3-NN	4-NN	5-NN	DT	NB
66.2	58.8	75.0	72.1	75.0	73.5	66.2

Data in table show that application of all features gives unsatisfactory results for all tested classifiers. Therefore it is appropriate to search for way to improve classification accuracy.

Firstly, the ANN classification accuracy was evaluated for single hidden neuron configuration. Results of the single layer configurations evaluation accuracy are summarized on figure 2.

The minimal accuracy among all 64 configurations was 82.4; maximal – 85.3; average – 83.96. The maximal accuracy was achieved by 16 different configurations and includes (13, 19, 20, 23, 27, 30, 31, 41, 43, 49, 50, 53, 56, 57, 62, 63) neurons in hidden layer. Overall the single hidden layer configuration has consistent results.

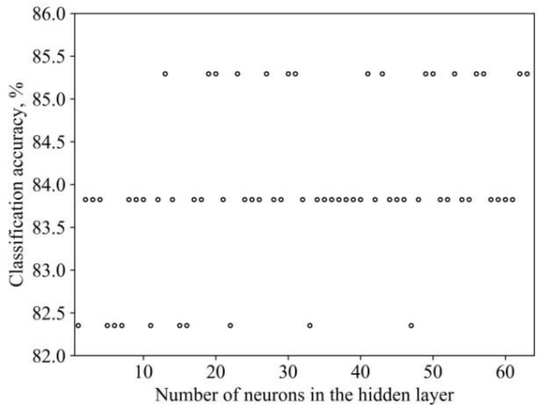

Figure 2: Single hidden layer classification accuracy.

Then, the possibilities of the two hidden layers configuration was evaluated. Results of the two layer configurations evaluation accuracy are summarized on figure 3.

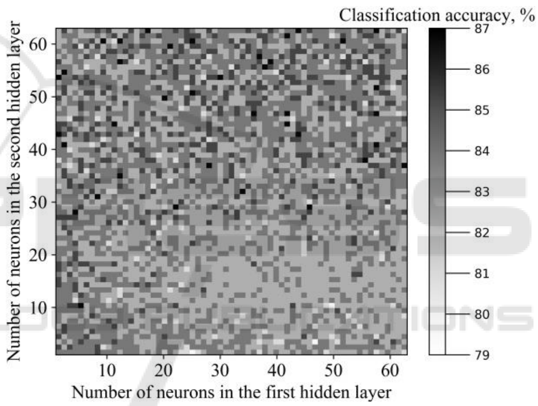

Figure 3: Two hidden layer classification accuracy.

The minimal accuracy among all 4096 configurations was 79.4; maximal – 86.8; average – 83.26. The maximal accuracy was achieved by 38 different configurations.

It is worthy to point out that, all configurations, studied in this work have shown result higher than simple classifiers while using all features. Obtained in this work accuracy is comparable with those presented in (Pytel et al., 2015). However, in mentioned work, the anthropometric features were used. This reduce application for the dynamic reaction evaluation to the neuro-electrostimulation.

It is worthy to point out that the highest accura-cy, when using only features in state F, was 72.1 %. This furthermore highlights the importance of the tilt-test in the arterial hypertension diagnosing.

However the overall accuracy can be still improved. One of the possible solutions is prior application of the efficient features selection.

4 DISCUSSIONS AND CONCLUSIONS

The present works shows results of the artificial neural networks application in task of the arterial hypertension diagnostics. The distinctive feature of the present work is application of the heart rate variability signals data recorded during tilt-test study. The vector of 64 time-domain, frequency-domain and non-linear features was used. The results, obtained in this work will become foundation of the decision support system in treatment of arterial hypertension.

Results of this study showed, that application of Artificial Neural Networks reaches higher classification accuracy results than such machine learning classifiers as discriminant analysis, Naïve Bayes, Decision Tree, Nearest Neighbors. Relatively high values of accuracy were obtained – 86.8. We want to point out that this work was the first step in the neural networks application study. In the following we are interested in continuing more complex networks that could perform prior features selection for accuracy improvement. One of the possible ways of the future development is usage of different networks architectures, like auto-encoding, for dimension reduction (Hinton and Salakhutdinov, 2006).

The next step in the development of the decision support system in treatment of arterial hypertension is evaluation of the treatment efficiency. We are planning to evaluate efficiency of the standard pharmacological therapy and neuro-electrostimulation by the 'SYMPATHOCOR-01' device. Such study will allow to estimate possibility of the proposed system application for evaluation of the treatment efficiency and prognosis of the treatment process.

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